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APPLICATION NO	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO	CONFIRMATION NO
09/944,929	08/31/2001	Kevin P. Baker	P2548PTC21	2450

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EXAMINER
LOEB, BRONWEN

ART UNIT	PAPER NUMBER
1636	4

DATE MAILED: 02/11/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/944,929	BAKER ET AL.	
	Examiner	Art Unit	
	Bronwen M. Loeb	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 August 2001 and 05 September 2002*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *22-41* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *22-41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *31 August 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☒ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 6.
4)☐ Interview Summary (PTO-413) Paper No(s). _____.
5)☐ Notice of Informal Patent Application (PTO-152)
6)☒ Other: *See Continuation Sheet*.

Continuation of Attachment(s) 6). Other: information regarding Copy of Papers Originally Filed.

DETAILED ACTION

This action is in response to the preliminary amendments filed 31 August 2001 and 5 September 2002. The 31 August 2001 amendment cancelled claims 1-21 and provided new claims 22-41. The 5 September 2002 amendment amended the priority data in the specification.

Claims 22-41 are pending.

Priority

1. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. § (120 or 119(e)) as follows:

The second application (which is called a continuing application) must be an application for a patent for an invention which is also disclosed in the first application (the parent or provisional application); the disclosure of the invention in the parent application and in the continuing application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. §112. See *In re Ahlbrecht*, 168 USPQ 293 (CCPA 1971).

Upon review of the specification of the parent (or provisional) application and comparison with the specification of the present application, it is determined that the specification of parent (or provisional) application 09/254,311 (the national stage application of PCT/US98/25108) is not enabling for the use of the instantly claimed invention. PCT/US99/28301 (published as WO 00/32776) is the first parent that

discloses the activity of inhibiting proliferation of stimulated T-lymphocytes. The specification of the 09/254,311 parent (or provisional) application does not teach or suggest an enabled use for the claimed nucleic acids. The specification of '311 teaches PRO361 is possibly a mucin or a chitinase, however any use based on these speculations is not enabled. Since PRO361's activity of inhibiting proliferation of stimulated T-lymphocytes is not disclosed in the parent (or provisional) application and cannot be predicted from the teachings of the parent (or provisional) application, the parent (or provisional) application is not enabling for the instantly claimed invention. Thus, the requirements of the first paragraph of 35 U.S.C. §112 have not been met. Accordingly, claims 22-41 are assigned an effective filing date of 1 December 1999.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. §112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 22-27, 30, 31 and 35-41 are rejected under 35 U.S.C. §112, first paragraph, because the specification, while being enabling for an isolated nucleic acid encoding a polypeptide having at least 80% sequence identity to the polypeptide of SEQ ID No. 83 or to the polypeptide lacking the signal peptide which polypeptide inhibits proliferation of stimulated T-lymphocytes, does not reasonably provide enablement for nucleic acids which encode a polypeptide having at least 80% sequence identity to SEQ ID No. 83 that do not have this activity. The specification does not

enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The specification identifies PRO361 as a polypeptide having homology to mucin and/or chitinase proteins (p. 109, lines 31-33) as well as having sequences typical of the arginase family of proteins (p. 109, lines 27-29). The specification however does not disclose if PRO361 actually is a mucin and/or a chitinase nor does it teach any use with respect to these possible identities. The only biological activity demonstrated is inhibition of proliferation of stimulated T-lymphocytes (p. 141, Example 34). It is unknown if the extracellular domain (which the Examiner assumes is about 26-383, based on Figure 32) alone would possess this biological activity. While one of skill in the art would be able, without undue experimentation, to use polypeptides with this biological activity, neither the specification nor the prior art adequately teaches how to use PRO361 derivatives without this biological activity.

In conclusion, based on the broad nature of the claims, the lack of sufficient guidance in the prior art or the specification, and the large quantity of experimentation required to find a use for polypeptides with unknown biological activity, it is concluded that enablement is limited to those nucleic acids encoding structural variants which inhibit proliferation of stimulated T-lymphocytes.

4. Claims 22-41 are rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable

one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The following factors have been considered in formulating this rejection (*In re Wands*, 858F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988): the breadth of the claims, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, the amount of direction of guidance presented, the presence or absence of working examples of the invention and the quantity of experimentation necessary.

The present claims are very broad. Claims 22, 27 and 25 encompass isolated nucleic acid encoding a polypeptide having at least 80% sequence identity to the polypeptide of SEQ ID No. 83, a polypeptide lacking the signal peptide, a polypeptide encoding the extracellular domain with or without the signal peptide, having the nucleotide sequence of SEQ ID No. 82 or having the nucleotide sequence of the cDNA in ATCC Accession number 209621.

The nature of the invention is an isolated nucleic acid encoding a polypeptide having the sequence of SEQ ID No. 83 and various structural variants. The specification generally teaches using nucleic acids for gene therapy (p. 73, lines 2-26) and that PRO361 polypeptides may be useful for in vivo therapeutic purposes (p. 81, lines 5-6).

An analysis of the prior art as of the effective filing date of the present application shows the complete lack of documented success for any treatment based on gene therapy. In a review on the current status of gene therapy, both Verma et al (Nature

(1997) 389:239-242) and Palù et al (J. Biotechnol. (1999) 68: 1-13) state that despite hundreds of clinical trials underway, no successful outcome has been achieved. See Verma et al, p. 239, 1st paragraph; Palù et al, p. 1, Abstract. The continued, major obstacles to successful gene therapy are gene delivery and sustained expression of the gene. Regarding non-viral methods for gene delivery, Verma et al indicates that most approaches suffer from poor efficiency and transient expression of the gene (p. 239, col. 3, 2nd paragraph). Likewise, Luo et al (Nature Biotechnology (2000) 18:33-37) indicates that non-viral synthetic delivery systems are very inefficient. See p. 33, Abstract and col. 1, 1st and 2nd paragraphs. While all three references indicate the promise of gene therapy, it is still a technique of the future and advancements in our understanding of the basics of gene delivery and expression must be made before gene therapy becomes a useful technique. See Verma et al, p. 242, col. 2-3; Palù et al, pp. 10-11; Luo et al , p. 33, col. 1, 1st paragraph.

The relative skill of those in the art of recombinant DNA techniques and medical treatments is high.

The area of the invention is unpredictable. As discussed above, the method of in vivo or ex vivo gene therapy is highly complex and unpredictable. Indeed, the recent tragic and unexpected death of a participant in a gene therapy clinical trial clearly illustrates the unpredictable nature of gene therapy. See Fox, ASM News, Feb. 2000, 66 (2): 1-3. More recently, two children treated with retroviral gene therapy for SCID have been diagnosed with leukemia, further indication of the unpredictable nature of gene therapy which persists to the current time. See Fox, Yahoo! News, January 14,

2003 (Accessed Jan. 14, 2003 from

http://news.yahoo.com/news?tmpl=story2&cid=570&u=/nm/20030114/sc_nm/health_genetherapy_dc&printer=1).

Furthermore, given that there is no evidence other than some sequence homology to demonstrate that PRO361 has an mucin and/or chitinase activity, it is entirely unknown, and therefore unpredictable, whether PRO361 would have any therapeutic value in any cancer or disorders involving cell surface molecules or receptors. The skilled artisan at the time the present invention was made recognized the difficulty of achieving sufficient heterologous gene expression to induce any therapeutic effect.

The present specification provides little or no guidance to support the claimed invention for gene therapy applications. The specification discloses no specific diseases for which the claimed isolated nucleic acids can be applied. There is no direction provided as to how to overcome the obstacles to gene therapy recognized by leaders in the field, i.e. low efficiency of gene delivery and transient gene expression.

The single working example disclosed shows that PRO361 can inhibit proliferation of stimulate T-lymphocytes.

The quantity of experimentation necessary to carry out the claimed invention is high as the skilled artisan could not rely on the prior art or the present specification to teach how to use the claimed methods. In order to determine how to use the method to treat a condition, one of skill in the art would have to determine whether PRO361 has mucin and/or chitinase activity, if there are any diseases or disorders which could be treated using such activity, the effect exogenous transgene expression would have in any cell type, whether the effect could be exploited for treatment of a disease, how to

deliver the given nucleic acid to the appropriate target cells with specificity and efficiency, and how to get sufficient expression to induce at least some therapeutic effect. Since neither the prior art nor the specification provides the answers to all of these questions, it would require a large quantity of trial and error experimentation by the skilled artisan to do so.

Based on the broad scope of the claims, the unpredictability in the area of the invention, the lack of sufficient guidance or working examples in the specification and the quantity of experimentation necessary, it would clearly require undue experimentation by one of skill in the art to determine how to use the claimed isolated nucleic acids encoding the polypeptide of SEQ ID No. 83 or variants thereof.

5. Claims 22-27 and 35-41 are rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The written description requirement is established by 35 U.S.C. 112, first paragraph which states that the: "*specification* shall contain a written description of the invention. . .[emphasis added]." The written description requirement has been well established and characterized in the case law. A specification must convey to one of skill in the art that "as of the filing date sought, [the inventor] was in possession of the invention." See *Vas Cath v. Mahurkar* 935 F.2d 1555, 1560 19 USPQ2d 1111, 1117 (Fed. Cir. 1991). Applicant may show that he is in "possession" of the invention claimed

by describing the invention with all of its claimed limitations "by such descriptive means as words, structures, figures, diagrams, formulas, etc., that fully set forth the claimed invention." See *Lockwood v. American Airlines Inc.* 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997).

This rejection is based on the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. §112, first paragraph "Written Description" Requirement published in the Federal Register (Volume 66, Number 4, Pages 1099-1111). The claims are drawn to an isolated nucleic acid 1) encoding a polypeptide having at least 80%, 85%, 90%, 95% or 99% sequence identity to the polypeptide of SEQ ID No. 83, 2) encoding a polypeptide having at least 80%, 85%, 90%, 95% or 99% sequence identity to the a polypeptide of SEQ ID No. 83 lacking the signal peptide, 3 and 4) encoding a polypeptide having at least 80%, 85%, 90%, 95% or 99% sequence identity to the a polypeptide of SEQ ID No. 83 encoding the extracellular domain with or without the signal peptide, 5) having the nucleotide sequence of SEQ ID No. 82, 6) having the full-length coding sequence of SEQ ID No. 82 or 7) having the nucleotide sequence of the cDNA in ATCC Accession number 209621. The claims do not recite that the polypeptide encoded by the nucleic acid possess any particular function, nor any particular conserved structure, or any other disclosed distinguishing feature. Thus the claims are drawn to a genus of nucleic acids that is defined only by sequence identity.

The specification mentions nucleic acid of SEQ ID No. 82 which encodes a polypeptide that has the activity of inhibiting proliferation of stimulated T-lymphocytes.

This disclosure is not deemed to be descriptive of the complete structure of a representative number of species encompassed by the claims as one of skill in the art cannot envision all of the isolated nucleic acids based on the teachings in the specification. The specification does not teach any correlation between any sequence and the biological activity of inhibiting proliferation of T-cell lymphocytes. There is no disclosure of the amino acids in the hydrophobic core of the protein essential to proper folding. Therefore, the specification does not describe the claimed the isolated nucleic acids in such full, clear, concise and exact terms so as to indicate that Applicant has possession of these isolated nucleic acids at the time of filing the present application. Thus, the written description requirement has not been satisfied.

Conclusion

Claims 22-41 are rejected.

Certain papers related to this application may be submitted to Art Unit 1636 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). The official fax telephone numbers for the Group are (703) 308-4242 and (703) 305-3014. NOTE: If Applicant does submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bronwen M. Loeb whose telephone number is (703) 605-1197. The examiner can normally be reached on Monday through Friday, from 11:00 AM to 7:30 PM. A phone message left at this number will be responded to as soon as possible (usually no later than the next business day after receipt by the examiner).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Remy Yucel, can be reached on (703) 305-1998.

The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Bronwen M. Loeb, Ph.D.
Patent Examiner
Art Unit 1636

February 9, 2003

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